REMARKS

In the Office Action, claim 297 was objected to under 35 USC 132. Claim 297 was also objected to on the basis of the informality "Tris-Cl". Claims 275-284 and 297 were rejected under 35 USC 112, first paragraph as lacking written description. Claims 225-244, 265-284, and 297 were rejected under 35 USC 112, first paragraph as lacking enablement. Claims 275 and 297 were rejected under 35 USC 112, second paragraph as indefinite. Claims 215-244, 255-284 and 297 were rejected for obviousness-type double patenting over claims 1 and 4-12 of U.S. Pat. No. 6,459,018.

Support for the amendments to the claims and specification can be found throughout the application as filed. No new matter is added. Amendments relating to the "coding region" of the nucleic acid find support at least at page 19, lines 27-28. Claim 300 invokes 35 USC Section 112, sixth paragraph; the means for forming the described monounsaturated bond encompasses the disclosed *M. alpina* sequence and structural equivalents derived therefrom, as permitted by the statute. Claims 298 and 299 find support in the specification and claims as filed, included the discussion of hybridizing to *Mortierella* species in the application, and the description of hybridization to the *M. alpina* libraries in Examples 1 and 2.

The objections to claim 297

Claim 297 was objected to under 35 USC 132 and on the basis of the informality of "Tris-Cl". Cancellation of claim 297 renders these objections moot. The specification has been amended above as requested.

The written description rejection

Claims 275-284 and 297 were rejected under 35 USC 112, first paragraph as lacking written description. Cancellation of these claims renders this rejection moot.

The enablement rejection

Claims 225-244, 265-284, and 297 were rejected under 35 USC 112, first paragraph as lacking enablement. Cancellation of claims 275-284 and 297 renders that portion of the rejection moot. The rejection is otherwise traversed.

> The examiner bears the initial burden of showing nonenablement. See In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

> "[E]nablement requires that the specification teach those in the art to make and use the invention without 'undue experimentation.' . . . That some experimentation may be required is not fatal; the issue is whether the amount of experimentation required is 'undue.'" In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) (emphasis in original). Some experimentation, even a considerable amount, is not "undue" if, e.g., it is merely routine, or if the specification provides a reasonable amount of guidance as to the direction in which the experimentation should proceed. See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Ex Parte Bandman, Appeal No. 2004-2319, Application No. 09/915,694, paragraph bridging pages 6-7 (overturning a rejection for lack of reasoning or evidence of nonenablement where the enablement rejection, as here, alleged a lack of specific teaching of exact mutants to be made and lack of a demonstrated structure-function relationship; nonprecedential).

As in *Bandman*, *Wands,* and *Wright*, because no reasoning or evidence has been provided as to how undue experimentation would be required to practice the claimed invention, *prima facie* enablement of the claims has not been established here.

This rejection appears to be based on a misinterpretation of what is required to enable the scope of a generic claim. It has never been a requirement that one must make all possible species falling within a generic claim. Broad claims have long been permitted in the pharmaceutical and polymer chemistry fields where huge numbers of individual species fall within the claim scope. As long as the range of species can be prepared using known techniques, such claims are enabled, and provide an appropriate scope of protection to incentivize invention. The law has similarly been applied in the biotechnological arts, where an applicant was required only to enable the production of one antibody having the claimed functional characteristics: "Wands carried out this entire procedure three times, and was successful each time in making at least one antibody that satisfied all of the claim limitations." *In re Wands,* 8 USPQ 2d 1400, 1407 (Fed. Cir. 1988), emphasis added.

MPEP Section 2164.08 states (emphasis added):

> The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without `undue experimentation'." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Nevertheless, not

> everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).
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> As concerns the breadth of a claim relevant to enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. In re Moore, 439 F.2d 1232, 1236, 169 USPQ 236, 239 (CCPA 1971).
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> The determination of the propriety of a rejection based upon the scope of a claim relative to the scope of the enablement involves two stages of inquiry. The first is to determine how broad the claim is with respect to the disclosure. The entire claim must be considered. The second inquiry is to determine if one skilled in the art is enabled to make and use the entire scope of the claimed invention without undue experimentation.
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> How a teaching is set forth, by specific example or broad terminology, is not important. In re Marzocchi, 439 F.2d 220, 223-24 169 USPQ 367 , 370 (CCPA 1971). ... In In re Goffe, 542 F.2d 564, 567, 191 USPQ 429, 431 (CCPA 1976), the court stated:
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> [T]o provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for "preferred" materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts.

Applicants are the first to disclose the *M. alpina* Δ6 desaturase DNA and protein sequences and the first to demonstrate and characterize the activity of the encoded protein. Applicants are entitled to claims which bear a reasonable relationship to the invention they have disclosed to adequately protect their invention. Restricting them to their preferred material would not serve the constitutional purpose of promoting progress in the useful arts. This rejection is contrary to MPEP 2164.08 and unconstitutional.

The claims at issue each recite biological molecules having a reasonable relationship to the disclosed invention. Each requires use of a molecule related to one of the disclosed inventions, either through homology, ability to hybridize, or by deletion. Each such generic

claim additionally requires that the encoded protein retain the function of ability to desaturate a fatty acid between carbons 6 and 7 as disclosed by Applicants. The claims thus each reasonably relate to the scope of the disclosure.

It is art recognized that modifications to characterized proteins can lead to functional variants. Numerous techniques are taught in the specification for creating variants of the disclosed sequences, as has been acknowledged. Applicants are not required to recite every possible variation. Applicants in the chemical and polymeric arts routinely obtain claims of enormous scope resulting from the number of permutations through which the various R groups or monomeric units, respectively, may be combined. They are not required to synthesize each individual variant to demonstrate embodiment, but rather must only be able to make embodiments spanning the scope of the invention. Typically such claims are limited by functional language requiring a particular activity for the disclosed structure, as has been done here with the desaturase activity for the generic claims.

Generic claims to antibodies were found enabled in *In re Wands*, with the claims limited only by functional characteristics regarding antibody class and binding affinity, even though the individual number of antibodies which can be produced through variability in genetic and immunological recombination includes vast numbers of possible structures, because one of skill following the teachings of *Wands* could produce <u>one</u> antibody meeting the claim limitations without undue experimentation. *Wands* at 1407.

Regarding new claims 298-299 and claims dependent thereon involving a hybridization limitation, these claims recite a standard against which the hybridization limitation can be measured. Hybridization to a *Mortierella* library is described in the specification, and in fact is how the claimed sequence was obtained in the experiments described in the application. Relative terminology is permitted, particularly where a standard is provided. See MPEP 2173.05(b and g). Here the standard requires that the hybridization conditions be suitable for selectively screening a recombinant library from *Mortierella*, or *M. alpina*, using the complement of SEQ ID NO: 1. Similarly, a limitation on a chemical compound as "incapable of forming a dye with said oxidizing developing agent" although functional, was perfectly acceptable because it set definite boundaries on the patent protection sought in reciting a standard against which a compound could be measured. *In re* Barr, 444 F.2d 588, 170 USPQ

33 (CCPA 1971), cited at MPEP 2173.05(g). Applicants here have provided a standard against which hybridization can be measured, in permitted functional language. Applicants assert that no more than two weeks experimentation would be required to determine the full range of hybridization conditions that meet this relative standard. This is not undue experimentation. The results would not encompass any hybridization conditions, as stated in the Office Action, and statements that one of skill could not determine what preferential hybridization is similarly lack sound scientific reasoning; the ability to determine preferential hybridization of nucleic acid sequences is one of the pillars of molecular biology.

Applicants have taught techniques that permit the practice of the full scope of the invention. In Examples 5-8, Applicants demonstrate the use of yeast expression and functional characterization of putative desaturase clones. Using the disclosed system at the time of invention, assuming without prejudice for the purposes of argument only that the earliest priority date is the date of invention, a technician of less than ordinary skill could have screened hundreds of mutants a week. This demonstrates the number of mutants from the disclosed sequences that could be screened following the teachings of the invention and the amount of experimentation necessary to practice the claimed invention.

Submitted herewith in the accompanying Information Disclosure Statement and incorporated herein by reference is Hill-Eubanks et al., "Structure of a G-Protein-Coupling domain of a Muscarinic Receptor Predicted by Random Saturation Mutagenesis," JBC 271(6):3058-3065, a publication demonstrating that one of skill could screen hundreds of mutants in a disclosed sequence and characterize their function using routine experimentation with techniques available at the time of the invention. Furthermore, that publication discloses the use of a functional assay in mammalian NIH3T3 cells to characterize the mutants, a much more labor intensive technique than the methods described in this application, which would permit screening of an even greater number of mutants.

The comments in the Office Action regarding the three-dimensional structure do not have any bearing on the enablement of the claims. The claims do not recite a three-dimensional structure. There is no requirement that Applicants disclose the three-dimensional structure of the desaturase. Nor must Applicants demonstrate obtaining sequences "from any biological source" that hybridize to the disclosed sequence to enable their claims.

The full scope of the invention can be practiced without such knowledge or experimentation. The high-throughput capable screening methods taught in the application could screen sufficient mutants to allow the analysis of multiple mutations, including deletions, at every residue of the disclosed sequence without undue experimentation, using techniques described in the application and known in the art.

The comments in the Office Action that assert the specification teaches away from a "naturally occurring 80% sequence homologues of SEQ ID NO: 1" because of a differing A/T content are similarly not relevant. The phrase "naturally occurring" is not a claim element. That the borage and *M. alpina* sequences are different is not surprising, and the statements in the Office Action only demonstrate the novelty of the claimed invention. One of skill could prepare an 80% (or 60%, 90%, or 95%) homologous functional sequence from the sequence taught in the application with routine experimentation.

No evidence or specific argument has been provided as to how much experimentation would be required to prepare one deletion mutant of, one hybridizing sequence to, or one protein with the recited homology to the *M. alpina* delta-6 desaturase with the described activity as recited in the claims.

Absent such evidence, and without an analysis of all the *Wands* factors for these claims, no *prima facie* case of non-enablement has been established. Only routine experimentation is required to practice the claimed invention in its full scope. Accordingly, the presented claims are fully enabled; the application teaches one of skill in the art how to make and use the full scope of the claimed invention.

The rejections under 35 U.S.C. §112, second paragraph

Claims 275 and 297 were rejected under 35 USC 112, second paragraph as indefinite. Cancellation of these claims renders these rejections moot.

The obviousness-type double patenting rejection

Claims 215-244, 255-284 and 297 were rejected for obviousness-type double patenting over claims 1 and 4-12 of U.S. Pat. No. 6,459,018. Cancellation of claims 275-284 and 297 renders that portion of the rejection moot. The rejection is otherwise traversed.

To establish obviousness, all claim elements must be contained in the cited reference(s). For an obviousness-type double patenting rejection, only the claims of the cited patent may be used to establish obviousness; the specification may not be used.

Cited claims 1 and 4-12 of the '018 patent relate to a method for producing stearidonic acid in a plant seed using a seed-specific promoter to express a delta-six desaturase. The pending claims relate to methods for producing oil with an altered fatty acid profile through microbial expression of a delta-six desaturase. The '018 patent claims do not teach or suggest microbial expression, and the recited seed-specific promoter in the '018 claims would not be expected to function in a microbial system as claimed here. Thus there was no reasonable expectation of success in modifying the claimed '018 invention for microbial expression.

As all claim elements are not present in the cited reference and there was no reasonable expectation of success, obviousness has not been established.

CONCLUSION

Applicants request reconsideration of the claims in view of the above amendments and remarks. A notice of allowance is earnestly solicited. If a telephone conference would expedite allowance of this matter, the Examiner is welcome to contact the undersigned.

If an appropriate payment does not accompany or precede this submission, the Commissioner is hereby authorized to charge any required fees, including any petition for extension of time, or to credit any overpayment, to Deposit Account No. 06-1135, billing reference no. 86014-8145.

Respectfully submitted,

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